FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE' ENTERED AT 20:58:58 ON 26 MAY 2008

L1 900 S PENETRATIN
L2 89 S L1 (P) TRANSDUC?
L3 34 DUP REM L2 (55 DUPLICATES REMOVED)
L4 229 S ANTENNAPEDIA (P) TRANSDUC?
L5 103 DUP REM L4 (126 DUPLICATES REMOVED)
L6 27 S L5 AND PY<=2002
L7 13 S L4 AND HYDROPHOBI?
L8 7 DUP REM L7 (6 DUPLICATES REMOVED)
L9 15 S L2 AND HYDROPHOBI?
L10 6 DUP REM L9 (9 DUPLICATES REMOVED)

AU Mittelman J M; Gudkov A V
SO Somatic cell and molecular genetics, (1999 May) Vol. 25, No. 3, pp. 115-28.
Journal code: 8403568. ISSN: 0740-7750.
TI Generation of p53 suppressor peptide from the fragment of p53 protein.
AB The p53 protein, encoded by a tumor suppressor gene, mediates growth arrest or apoptosis in response to a variety of stresses. p53-dependent apoptosis, occurring in several sensitive tissues after radiation or chemotherapy, is partially responsible for the side effects of cancer treatment, making p53 a potential target for therapeutic suppression. p53 function can be suppressed by the ectopic expression of p53-derived peptides, isolated earlier using functional selection of genetic suppressor elements (GSEs) from a library of randomly fragmented p53 cDNA (Ossovskaya et al. [1996]. Proc. Natl. Acad. Sci. U.S.A. 93, 10309). The potent p53-suppressing GSE, GSE56, had been used to generate in an E. coli expression system a peptide with anti-p53 activity by fusion of the GSE-encoded sequence with penetratin, a 16-amino-acid-long peptide capable of efficient translocation through cell membranes. Fusion with penetratin does not affect the anti-p53 activity of retrovirus-transduced GSE56. The fused peptide was able to attenuate p53-mediated transactivation and apoptosis when added into culture media. Interestingly, GSE56-derived peptide with no penetratin also had accumulated in the cells and showed similar, though lower, anti-p53 activity. This study provides the rationale and methodological basis for efficient generation of biologically active peptides with therapeutic potential from GSEs isolated through functional selection.

AU Han K; Jeon M J; Kim K A; Park J; Choi S Y
SO Molecules and cells, (2000 Dec 31) Vol. 10, No. 6, pp. 728-32.
Journal code: 9610936. ISSN: 1016-8478.
TI Efficient intracellular delivery of GFP by homeodomains of Drosophila Fushi-tarazu and Engrailed proteins.
AB The 60 amino acid long homeodomain of Antennapedia (Antp), either alone or as a fusion protein with 30-40 amino acid long foreign polypeptides, has been reported to cross biological membranes by an energy- and receptor-protein-independent mechanism. Moreover, the 16 amino acid long third helix of the Antp homeodomain, so-called penetratin, possesses translocation properties when fused to fewer than 100 amino acids as well. These findings led us to study whether such a protein tansduction property is shared by other homeodomains. We report here that homeodomains of two homeoproteins, Fushi-tarazu and Engrailed, are able to transduce a 238 amino acid long green fluorescent protein into cultured cells as efficiently as other well-known protein transduction domains, such as an internal oligopeptide of Tat and penetratin. These findings suggest that such transduction activity of homeodomains might have some physiological roles and that it can be exploited for development of efficient transduction vectors for research use and protein therapy.

AU Dunican D J; Doherty P

SO Biopolymers, (2001) Vol. 60, No. 1, pp. 45-60. Ref: 97
Journal code: 0372525. ISSN: 0006-3525.

TI Designing cell-permeant phosphopeptides to modulate intracellular signaling pathways.

AB A central theme in intracellular signaling is the regulatable interaction of proteins via the binding of specialized domains on one protein to short linear sequences on other molecules. The capability of these short sequences to mediate the required specificity and affinity for signal transduction allows for the rational design of peptide-based modulators of specific protein-protein interactions. Such inhibitors are valuable tools for elucidating the role of these interactions in cellular physiology and in targeting such interactions for potential therapeutic intervention. This approach is exemplified by the study of the role of phosphorylation of specific sites on signaling proteins. However, the difficulty of introducing large hydrophilic molecules such as phosphopeptides into cells has been a major drawback in this area. This review describes the application of recently developed cell-permeant peptide vectors in the introduction of biologically active peptides into cells, with particular emphasis on the antennapedia/penetratin, TAT, and signal-peptide based sequences. In addition, the modification of such peptides to increase uptake efficiency and affinity for their targets is discussed. Finally, the use of cell-permeant phosphopeptides to both inhibit and stimulate intracellular signaling mechanisms is described, by reference to the PLCgamma, Grb2, and PI-3 kinase pathways.

AU Li Yin; Rosal Ramon V; Brandt-Rauf Paul W; Fine Robert L

SO Biochemical and biophysical research communications, (2002 Nov 1) Vol. 298, No. 3, pp. 439-49.
Journal code: 0372516. ISSN: 0006-291X.

TI Correlation between hydrophobic properties and efficiency of carrier-mediated membrane transduction and apoptosis of a p53 C-terminal peptide.

AB Two membrane transporters, the 17 amino acid (aa) oligopeptide penetratin derived from the homeodomain of Antennapedia (Ant) and an analogue of the basic domain of TAT (aa 47-57) (TAT-a) from HIV-1, were tested as carriers for a p53 C-terminal peptide (aa 361-382) into human breast cancer cells. The studies were performed to determine whether the membrane-transduction efficiency of membrane carriers: Ant, TAT or TAT analogue (TAT-a) correlated with peptide hydrophobic features. Peptide-sequence analysis clearly demonstrated that the Ant sequence and p53 peptide sequence (p53p) together created a peptide with enhanced hydrophobic characteristics; while the TAT or TAT analogue (TAT-a) and p53p sequence together created a peptide with significantly less hydrophobic qualities. The degree of hydrophobic moment and helical wheel plots for these peptides correlated directly with their ability to transduce the p53 peptide. Western blot analysis revealed that Ant was able to transduce p53 C-terminal peptide into human breast cancer cells as a highly efficient membrane transporter. Compared to Ant, TAT-a fused to the C-terminus of p53 peptide (p53p-TAT-a) was a less efficient carrier into these cells under the conditions of our study. Additionally, N-terminal linked TAT-a to p53p (TAT-a-p53p) showed even lower efficiency as a transporter than p53-TAT-a. Apoptosis assays showed that the p53 peptide, fused at its C-terminus to Ant (p53p-Ant), induced a higher percentage of apoptotic cells in human breast cancer cell lines expressing mutant or wild-type p53 as compared to p53 peptide fused at its C-terminus to the TAT-a sequence (p53p-TAT-a) or when fused at the N-terminus to TAT-a (TAT-a-p53p). These data suggested a direct correlation between hydrophobic characteristics and efficiency as a transporter. Sequence study, using hydrophobic moment and helical wheel analyses, may be useful predictive tools for choosing the best carrier for a peptide.

AU Lindsay, Mark A.
SO Current Opinion in Pharmacology (2002), 2(5), 587-594
CODEN: COPUBK; ISSN: 1471-4892
TI Peptide-mediated cell delivery: application in protein target validation
AB A review. Recent reports have suggested that conjugation of peptides, proteins and antisense to short highly basic peptides, such as TAT, antennapedia and transportan, results in their rapid translocation into cells. Importantly, these conjugates have been shown to exert actions in a no. of animal models suggesting their general utility for the detn. of protein function in vitro and in vivo. Could protein transduction domains provide a universal in vitro and in vivo delivery system for the identification of protein function.

AU Hall H; Williams E J; Moore S E; Walsh F S; Prochiantz A; Doherty P
SO Current biology : CB, (1996 May 1) Vol. 6, No. 5, pp. 580-7.
Journal code: 9107782. ISSN: 0960-9822.
TI Inhibition of FGF-stimulated phosphatidylinositol hydrolysis and neurite outgrowth by a cell-membrane permeable phosphopeptide.
AB BACKGROUND. Activated receptor tyrosine kinases bind downstream effector molecules with high affinity. Provided that they can be introduced into cells, peptides corresponding to these high-affinity sites should be able to compete for the interaction and thereby inhibit specific signal transduction cascades. The high-affinity binding site for phospholipase C gamma (PLCgamma) on the activated fibroblast growth factor receptor (FGFR) is centred around the tyrosine at position 766 (766Tyr), and peptides corresponding to this site inhibit PLCgamma binding to the receptor in vitro. A 16 amino-acid peptide from the third helix of the Antennapedia homeodomain protein has recently been shown to be able to act as an internalization vector that can deliver other peptides into cells. Here, we have designed a peptide that contains both the internalization sequence and the FGFR high-affinity binding site for PLCgamma, and tested it in cultures of cerebellar neurons for its ability to inhibit the activation of PLCgamma by basic FGF. RESULTS. The peptide containing the FGFR high-affinity binding site for PLCgamma inhibited phospholipid hydrolysis stimulated by basic FGF with a maximal effect at 1 microg ml-1. Phosphorylation of 766Tyr was required for this effect. The phosphorylated peptide had no effect on phospholipid hydrolysis stimulated by platelet-derived growth factor, neurotrophin-3 and bradykinin. The phosphorylated peptide also inhibited neurite outgrowth stimulated by FGF, but had no effect on neurite outgrowth stimulated by agents that activate the FGFR signal transduction cascade downstream from the activation of PLCgamma. CONCLUSIONS. Cell-permeable peptides can be designed that inhibit the function of receptor tyrosine kinases. In this context we have developed a peptide that prevents the FGFR from activating PLCgamma, and have used this peptide to obtain the first direct evidence that activation of PLCgamma is required for the neurite outgrowth response stimulated by basic FGF.

AU Ford K G; Souberbielle B E; Darling D; Farzaneh F
SO Gene therapy, (2001 Jan) Vol. 8, No. 1, pp. 1-4. Ref: 34
Journal code: 9421525. ISSN: 0969-7128.
TI Protein transduction: an alternative to genetic intervention?.
AB Protein transduction, an emerging technology with potential applications in gene therapy, can best be described as the internalisation of proteins into the cell, from the external environment. This process relies on the inherent property of a small number of proteins and peptides of being able to penetrate the cell membrane. The transducing property of these molecules can be conferred upon proteins which are expressed as fusions with them and thus offers an alternative to gene therapy for the delivery of therapeutic proteins into target cells. This review describes the three most commonly used protein transduction vehicles; the antennapedia peptide, the herpes simplex virus

VP22 protein and HIV TAT protein transduction domain. The future prospects for the application of this technology in gene therapy are also discussed.

AU Morris M C; Depollier J; Mery J; Heitz F; Divita G
SO Nature biotechnology, (2001 Dec) Vol. 19, No. 12, pp. 1173-6. Journal code: 9604648. ISSN: 1087-0156.
TI A peptide carrier for the delivery of biologically active proteins into mammalian cells.
AB The development of peptide drugs and therapeutic proteins is limited by the poor permeability and the selectivity of the cell membrane. There is a growing effort to circumvent these problems by designing strategies to deliver full-length proteins into a large number of cells. A series of small protein domains, termed protein transduction domains (PTDs), have been shown to cross biological membranes efficiently and independently of transporters or specific receptors, and to promote the delivery of peptides and proteins into cells. TAT protein from human immunodeficiency virus (HIV-1) is able to deliver biologically active proteins in vivo and has been shown to be of considerable interest for protein therapeutics. Similarly, the third alpha-helix of Antennapedia homeodomain, and VP22 protein from herpes simplex virus promote the delivery of covalently linked peptides or proteins into cells. However, these PTD vectors display a certain number of limitations in that they all require crosslinking to the target peptide or protein. Moreover, protein transduction using PTD-TAT fusion protein systems may require denaturation of the protein before delivery to increase the accessibility of the TAT-PTD domain. This requirement introduces an additional delay between the time of delivery and intracellular activation of the protein. In this report, we propose a new strategy for protein delivery based on a short amphipathic peptide carrier, Pep-1. This peptide carrier is able to efficiently deliver a variety of peptides and proteins into several cell lines in a fully biologically active form, without the need for prior chemical covalent coupling or denaturation steps. In addition, this peptide carrier presents several advantages for protein therapy, including stability in physiological buffer, lack of toxicity, and lack of sensitivity to serum. Pep-1 technology should be extremely useful for targeting specific protein-protein interactions in living cells and for screening novel therapeutic proteins.

AU Li Yin; Rosal Ramon V; Brandt-Rauf Paul W; Fine Robert L
SO Biochemical and biophysical research communications, (2002 Nov 1) Vol. 298, No. 3, pp. 439-49. Journal code: 0372516. ISSN: 0006-291X.
TI Correlation between hydrophobic properties and efficiency of carrier-mediated membrane transduction and apoptosis of a p53 C-terminal peptide.
AB Two membrane transporters, the 17 amino acid (aa) oligopeptide penetratin derived from the homeodomain of Antennapedia (Ant) and an analogue of the basic domain of TAT (aa 47-57) (TAT-a) from HIV-1, were tested as carriers for a p53 C-terminal peptide (aa 361-382) into human breast cancer cells. The studies were performed to determine whether the membrane-transduction efficiency of membrane carriers: Ant, TAT or TAT analogue (TAT-a) correlated with peptide hydrophobic features. Peptide-sequence analysis clearly demonstrated that the Ant sequence and p53 peptide sequence (p53p) together created a peptide with enhanced hydrophobic characteristics; while the TAT or TAT analogue (TAT-a) and p53p sequence together created a peptide with significantly less hydrophobic qualities. The degree of hydrophobic moment and helical wheel plots for these peptides correlated directly with their ability to transduce the p53 peptide. Western blot analysis revealed that Ant was able to transduce p53 C-terminal peptide into human breast cancer cells as a highly efficient membrane transporter. Compared

to Ant, TAT-a fused to the C-terminus of p53 peptide (p53p-TAT-a) was a less efficient carrier into these cells under the conditions of our study. Additionally, N-terminal linked TAT-a to p53p (TAT-a-p53p) showed even lower efficiency as a transporter than p53-TAT-a. Apoptosis assays showed that the p53 peptide, fused at its C-terminus to Ant (p53p-Ant), induced a higher percentage of apoptotic cells in human breast cancer cell lines expressing mutant or wild-type p53 as compared to p53 peptide fused at its C-terminus to the TAT-a sequence (p53p-TAT-a) or when fused at the N-terminus to TAT-a (TAT-a-p53p). These data suggested a direct correlation between hydrophobic characteristics and efficiency as a transporter. Sequence study, using hydrophobic moment and helical wheel analyses, may be useful predictive tools for choosing the best carrier for a peptide.